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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Podos et al.

Serial No.: 09/073,552 Examiner: Fay, Z.

Filed: May 6, 1998 Group Art Unit: 1644

For: 8-ISO-PROSTAGLANDINS FOR GLAUCOMA THERAPY

RESPONSE TO OFFICIAL ACTION

I hereby certify that this paper is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Assistant Commissioner of Patents, Washington, D.C., 20231, on

May 4, 1999

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Signature

May 4, 1999
Date of Signature

Assistant Commissioner of Patents
Washington, D.C. 20231

SIR:

In response to the Official Action dated February 4, 1999, please consider the following remarks.

Claims 1-21 are pending and are rejected under 35 U.S.C. §103 as obvious over United States Patent No. 5,631,287 by Schneider (henceforth "Schneider"). According to the Examiner, Schneider teaches the use of the claimed prostanoids for the treatment of glaucoma, and makes clear that the claimed type of prostaglandins have been previously used for the claimed purpose. The Examiner states that Applicants have presented no evidence to establish the unexpected or unobvious nature of the claimed invention.

In response, Applicants assert that the prostaglandins used by Schneider are

chemically and functionally different from those provided for in the instant claims. Schneider relates to derivatives and analogs of prostanoic acid with a geometric structure shown in their formula 1 (at column 2 line 27). This structure shows that the #8 carbon is in the α-configuration (by convention, below the plane of the 5-membered ring as drawn) and the #12 carbon in the opposite, or "β" configuration. This creates a "trans" structural relationship between the alpha and omega side chains. Exemplary specific compounds listed by Schneider (compounds 1-32 at column 4 line 14 through column 5 line 62) all share this trans geometric arrangement, as do all the structural formulas shown in the Schneider patent.

By contrast, the instant invention involves isomeric prostaglandin compounds in which both the #8 and #12 carbon atoms are in the β configuration, such that the side chains have a "cis", rather than a "trans", structural relationship. There is a great difference in three dimensions between these structural types of prostaglandin. In the trans arrangement (exhibited, for example, by the drug Latanoprost) the side chains diverge from the plane of the 5-membered ring to give a Y-shaped structure whereas in the cis arrangement the sidechains are parallel and have an L-shaped structure in space. This would suggest that the receptor-binding character is very different between these two structures. Indeed, the instant specification discloses the functional differences between the trans compound Latanoprost and the cis compounds of the invention. Latanoprost lowers intraocular pressure by increasing the outflow of aqueous humor via the uveoscleral route (in the instant specification at page 3 lines 9-14), whereas the claimed cis compound 8-isoPGE$_2$ lowers intraocular pressure primarily by decreasing the resistance to trabecular outflow of aqueous humor (in the instant specification at page 4 lines 2-6).

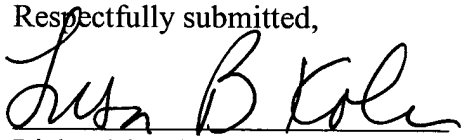
Data recently obtained by Applicants further supports the premise that Latanoprost and 8-iso-PGE$_2$ are functionally different. As indicated by the attached abstract, to be presented at the Association for Vision and Ophthalmology in May 1999, maximal doses of 8-isoPGE$_2$ and Latanoprost administered together gave a greater intraocular pressure ("IOP") response than when each drug ws given separately. This additivity supports the findings set forth

in the specification that each agent has a separate mechanism to lower IOP in the eye, and confirms that the mechanisms for 8-iso prostaglandins are different from Latanoprost and related prostaglandins with conventional geometric structure. If deemed necessary by the Examiner, Applicants will furnish a Declaration under 37 C.F.R. §132 in this regard.

Therefore, the compounds disclosed in Schneider are structurally and functionally different from those provided for in the instant claims. Accordingly, Schneider cannot be considered to render the claims obvious, and the rejection should be removed.

An early allowance is earnestly requested.

Respectfully submitted,



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